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Elizabethkingia meningoseptica: A new cause of ventilator-associated pneumonia in pediatric intensive care unit

The elizabethkingia meningoseptica

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Abstract
Aim: Ventilator-associated pneumonia (VAP) is diagnosed by detecting bacterial microorganisms in addition to purulent tracheal secretions, fever, respiratory distress, leukocytes in the tracheal aspirate, and radiological findings of pneumonia in patients on mechanical ventilation for more than 48 hours. The objective of this study was to determine the effects of E. meningoseptica bacteria and other agents, which are infrequently detected in tertiary pediatric intensive care units, on clinical findings, demographic characteristics, and mortality in patients with VAP.
Material and Methods: In this retrospective study, patients who were intubated in a tertiary pediatric intensive care unit (PICU) and diagnosed with ventilator-associated pneumonia according to CDC criteria between 2021 and 2022 were evaluated. The study included 42 patients who met all inclusion criteria.
Results: The 42 participants in the study were diagnosed with VAP based on CDC criteria and positive microbiological test results. The average age of the patients was 38,5 months, and the bmales predominated. Nine patients had E. meningoseptica isolated from them. Eight of the forty-two patients included in the investigation perished, and three of them had VAP. Mechanical ventilation time (p = 0.017) and PICU hospitalization time (p = 0.017) were both prolonged in the E. meningoseptica-isolated group.
Discussion: In recent years, the prevalence of E. meningoseptica infection in pediatric intensive care units has increased rapidly. This infection causes fatal opportunistic infections in patients receiving broad-spectrum antibiotics, followed by central venous catheters, duration of mechanical ventilation, and length of PICU stay.

Keywords
Ventilator-Associated Pneumonia, Elizabethkingia Meningoseptica, Antibiotics, Pediatric Intensive Care Unit

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Introduction

The term ventilator-associated pneumonia (VAP) refers to pneumonia that develops in patients who have been on mechanical ventilation for more than 48 hours [1]. The diagnosis is established clinically by detecting bacterial microorganisms along with purulent tracheal secretions, fever, respiratory distress, and white blood cells in the tracheal aspirate and detecting the radiological findings of pneumonia. It is one of the most important causes of hospital-acquired infections. Despite advances in asepsis techniques, antibiotic therapy, and supportive care, it is one of the causes of morbidity and mortality in intensive care patients. The incidence of VAP was found to be 9.62% in developed countries and 22.9% in developing countries [2,3]. Despite a better understanding of VAP risk factors, the incidence is still high. In a study conducted in developing countries, the mortality of VAP was 22%, 42.4%, and in studies conducted in developed countries, mortality was 18.4% [4,5,6].

Elizabethkingia meningoseptica (E.meningoseptica) is an oxidase-positive, non-glucose-fermenting, rod-shaped gram-negative bacterium commonly found in nature [7]. It is a rare pathogen that causes infections, especially in immunocompromised patients, such as neonatal meningitis, pneumonia, bacteremia, sepsis, soft tissue infections. The mode of transmission is not well known, it is stated that it is transmitted through contaminated water, and it usually causes hospital infections. The presence of invasive equipment, such as intravascular catheters, endotracheal tubes, and prosthetic devices, is most associated with prolonged treatment with broad-spectrum antibiotics, prolonged hospitalization, and nosocomial outbreaks [8].

Our aim in the study was to determine the effects of E. meningoseptica bacteria and other agents, which are rarely detected in a tertiary pediatric intensive care unit, on clinical findings, demographic characteristics, and mortality in VAP patients. E. meningoseptica is a rarely isolated agent that causes epidemics and is not frequently seen in pediatric intensive care units. The increase in the reporting of E.meningoseptica in adult intensive care units is a warning in terms of attention in terms of E.meningoseptica infections in PICUs in the future. There may be an increased risk for nosocomial infections in patients who are followed up in E.meningoseptica, PICUs, and who are usually immunosuppressed and undergo invasive intervention.

Material and Methods

Study Settings

The Institutional Ethical Committee of Bakırçay University, Türkiye, approved this retrospective, single-center study (approval number: 720/2022-GOA). Patients diagnosed with ventilator-associated pneumonia based on CDC criteria and followed as intubated in the tertiary pediatric intensive care unit (PICU) of Manisa City Hospital between 2021 and 2022 were evaluated retrospectively in this study. Our unit has twelve beds and admits more than 300 patients per year. All patient accommodations feature a single bed. On-call personnel include a pediatric intensive care specialist and a pediatrician. The ratio of nurses to patients is 1 to 1. The unit utilizes Maquet and Biovent-brand ventilators. Each patient uses a disposable active or passive humidifier circuit. Using an aerochamber device, patients receive inhaled therapy.

The investigation included patients who were followed in the intensive care unit between February 2021 and October 2022, were one month to eighteen years old, were on mechanical ventilation for more than 48 hours, and received endotracheal aspiration material. Patients who were mechanically ventilated for less than 48 hours and did not meet CDC criteria were excluded from the study.

Data gathering

PRISM score, laboratory data (maximum and minimum white cell count), duration of mechanical ventilation, length of stay in the pediatric intensive care unit, chest radiography results (new infiltration, consolidation, or cavity development), and culture results (endotracheal aspiration material) were collected retrospectively. All patients were monitored until discharge or exit for the development of ventilator-associated pneumonia.

Patients were diagnosed with VAP based on the following Centers for Disease Control and Prevention (CDC) criteria: 1-fever, leukopenia, or leukocytosis (any of them), 2-a-cough, dyspnea, or tachypnea; b-new onset; increasing or changing character of purulent secretion; c-lung on auscultation; ral or rhonchi; d-increased oxygen requirement or hypoxemia; 3-New onset or increased infiltration on radiography, consolidation (any of them), and 4-105 colony growth in endotracheal aspirate material (at least one of all four criteria is positive) [available from: https://www.cdc.gov]. Those with a positive endotracheal aspirate culture (ETA) below the threshold and those without clinical and radiological VAP findings were deemed colonized and excluded from the study.

Due to clinical findings, ETA was obtained from patients suspected of having VAP. In the interim, piperacillin-tazobactam was administered to the patients until their ETA results were determined. In ETA culture results, ceftazidime avibactam, or kinolon were added to patients with E. meningoseptica according to antibiogram results; inhaled antibiotics were added to some patients (especially gentamicin or colistin in patients with high renal function tests according to ETA antibiogram results); and intravenous antibiotic revision was performed on some patients. During the research period, 386 out of 962 intubated pediatric intensive care unit patients were followed up and included in the study. We excluded 198 intubated patients because they were connected to a mechanical ventilator for less than 24 hours and 24 patients because their medical records were insufficient. In 77 of 188 patients, VAP was considered, and ETA was sent. 105 colonies of colony growth were detected in the microbiological samples of 28 patients, and these patients were excluded from the study due to the possibility of ventilator-associated tracheitis. Twelve patients who met the CDC criteria were excluded from the study because the microbiological examination revealed no growth. The study included 42 patients who met all inclusion criteria.

Statistical analysis

For qualitative variables, data were analyzed using frequency and percentage (%), and for quantitative variables, mean standard deviation (SD), median, minimum, and maximum values were employed.E.meningoseptica and other microbiologic isolate groups were compared using the Mann-Whitney U test, Pearson

Chi-square test, Fisher's Exact test, and Fisher-Freeman-Alton test because the data did not exhibit a normal distribution. IBM-SPSS version 21.0 was used for statistical analyses, and p0.05 was considered significant.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

Forty-two study participants were diagnosed with VAP based on CDC criteria and positive microbiological test results. The average age of the patients was 38,5 months, males predominated. Respiratory diseases were the leading cause of PICU hospitalization and the most prevalent underlying disease. Eight of the forty-two patients included in the investigation perished, and three of them had VAP (Table 1).

Pseudomonas aeruginosa and Elizabethkingia meningoseptica were the most frequently isolated microorganisms in VAP patients. P. aeruginosa was isolated twice from a single patient, while E. meningoseptica was isolated twice from three patients (Table 2).

Males comprised 4 of the 9 patients isolated with E. meningoseptica and 19 of the 33 patients isolated with other microorganisms. According to CDC criteria, there was no statistically significant difference between the two categories. Mechanical ventilation time (p = 0.017) and PICU hospitalization time (p = 0.017) were both prolonged in the E. meningoseptica-isolated group. All patients in the E. meningoseptica-isolated group received intravenous antibiotics, while 14 patients in the other group received inhaled antibiotics. One patient isolated with E.meningoseptica and seven patients isolated with other microorganisms perished (Table 3).

Table 1. Patients' characteristics of diagnosis with ventilator-associated pneumonia.

Variables	Total (n=42)
Sex M/F n, (%)	23/19 (54.8/45.2)
Age (month) median, (IQR)	38.5 (12-124)
PRISM 3 score, median, (IQR)	15.5 (12- 24)
PICU admission diagnoses n, (%)	
Respiratory	28 (66.7)
Infection disease	10 (23.8)
Neuromuscular/Trauma	3 (7.1)
Cardiovascular	1 (2.4)
Comorbidities, n (%)	
Neurometabolic	19 (45.2)
Respiratory	12 (28.6)
Cardiovascular	5 (11.9)
Duration of mechanical ventilation (days), median (IQR)	24 (13.5- 36.2)
Length of PICU stay (days), median (IQR)	30.5 (18- 44.2)
PICU mortality, n (%)	
VAP-related	3 (7.1)
Other cause	5 (11.9)

Abbreviations: M: Male, F: Female, PRISM 3 score: Pediatric Risk of Mortality

Table 2. Pathogens isolated in the endotracheal aspirate.

Microorganisms	Total (n=48)
Pseudomonas aeroginosa	17 (38.1)
Elizabethkingia meningoseptica	12 (21.4)
Acinetobacter baumani	7 (16.7)
Klebsiella pneumonia	7 (11.9)
Serratia marcescens	3 (7.1)
Stenotrophomonas maltophilia	2 (4.8)

Table 3. Comparison of baseline demographic and clinical characteristics of the study patients.

Characteristics	Elizabethkingia meningoseptica (n=9)	Other microorganism (n=33)	P value
Sex M/F, n (%)	4/5 (44.4/55.6)	19/14 (57.6/42.4)	0.488
Age (month) median, (IQR)	36 (7-126)	42 (18-128)	0.416
PRISM 3 score median, (IQR)	15 (12-24)	16 (12-24)	0.674
CDC criteria n (%)			
Fever	7 (77.8)	17 (51.5)	0.163
Leukocyte count			
<4000/mm³	2 (22.2)	7 (21.2)	0.764
4000-15.000/mm³	3 (33.3)	9 (27.3)	
>15.000/mm³	4 (44.4)	17 (51.5)	
Dyspnea/tachypnea/cough	7 (77.8)	24 (72.7)	0.763
Rales or bronchial breath sounds	4 (44.4)	17 (51.5)	0.710
Increased respiratory secretions/ purulent sputum	9 (100)	29 (87.9)	0.278
Increased oxygen requirements or hypoxemia	5 (55.6)	11 (33.3)	0.319
Chest X-ray			
Consolidation	5 (55.6)	14 (42.4)	0.354
New infiltration	3 (33.3)	14 (42.4)	
Progressive infiltration	1 (11.1)	2 (6.1)	
Use of intravenous antibiotics, n (%)	9 (100)	19 (57.6)	0.018
Duration of mechanical ventilation (days), median (IQR)	32 (27-70)	22 (12-34.5)	0.017
Length of PICU stay (days), median (IQR)	44 (33.5-88)	28 (17-37)	0.017
PICU Mortality, n (%)			
VAP-related	1 (11.1)	2 (6.1)	0.433
Other cause	N/A	5 (15.2)	

Abbreviations: Other microorganism: Pseudomonas aeruginosa, Acinetobacter baumani, Klebsiella pneumonia, Serratia marcescens. PRISM 3 score: Pediatric Risk of Mortality

Discussion

In our study, we retrospectively analyzed 42 patients aged 0-18 years who were intubated in the PICU between 2021 and 2022 and diagnosed with ventilator-associated pneumonia according to CDC criteria. Patients' demographic information, microbiological results, and treatments were evaluated.

In established nations, the incidence of ventilator-associated pneumonia is 15-17%, whereas in developing nations, this rate is 25-35% [9,10]. A study found that the incidence of VAP was 11.6% per 1000 ventilator days [11]. It has been shown that PRISM scores of 10 or higher increase the incidence of VAP in pediatric intensive care patients following cardiac surgery [12]. In our investigation, the VAP rate per 1000 ventilator days was 29.2%. The VAP mortality rate is 5% in advanced units utilizing the VAP prevention bundles and 47.43% in developing units not utilizing the VAP prevention bundles. This rate was discovered to be 19% in our study. The use of VAP prevention bundles has just begun in our unit. We believe this rate will decrease as a

result of the implementation of VAP prevention packages.

P. aeruginosa (55%) and A. baumanni (31%) are the most frequently isolated microorganisms from cultures of endotracheal aspirate in pediatric intensive care units [13]. Similarly, P.aeroginosa was the most frequently detected microorganism in our study, followed by E.meningoseptica. Rarely detected in pediatric intensive care facilities, E. meningoseptica was isolated from 9 patients and 12 cultures in our study. Elizabethkingia meningoseptica is a gram-negative bacillus that causes nosocomial infections and is resistant to commonly used antibiotics in intensive care settings. The most prevalent clinical presentation of E.meningoseptica in children, according to a literature review spanning the years 1994 to 2017, was meningitis (73.9%), and admission with pneumonia was estimated to be 6.7% [14]. Premature infants, immunosuppressed patients, patients taking antibiotics, intensive care unit patients, and patients undergoing dialysis are susceptible to E. meningoseptica infections [15]. E. meningoseptiva was identified as a VAP agent among gram-negative bacteria in 8.66% of intensive care unit patients [16]. In our study, patients with VAP had a high prevalence of 21.4%. Recent years have witnessed the emergence of E. meningoseptica infection as a global emergent infectious disease with poor prognoses. PICU length of stay, underlying comorbidities, and the use of central venous catheters are risk factors for E. meningoseptica infection [16]. Our patients stayed longer in the PICU, but this may be due to E. meningoseptica, a difficult-to-eradicate multidrug-resistant microorganism. Six out of eight patients had neurometabolic disease comorbidity. Both underlying comorbidity and prolonged ICU stay increased the risk of E.meningoseptica infection in patients. Six of the patients who stayed longer than 32 days in the PICU were fitted with central venous catheters.

The majority of reported epidemics of E.meningoseptica in children occur sporadically. Infection with E. meningoseptica is preventable, whether sporadic or concentrated. The causative agent for the E.meningoseptica outbreak, which was detected in 30 patients in the adult intensive care unit, was found in the unit's water [17]. In our study, the majority of E.meningoseptica-isolated patients were admitted to the PICU at distinct times. E. meningoseptica was not detected in samples taken from areas where microorganisms can colonize, such as the water in the intensive care unit, aspiration materials, oxygen humidifiers, and distilled water used in mechanical ventilators.

E.meningoseptica is known to be antibiotic-resistant. In vitro, E.meningoseptica has been shown to be susceptible to fluoroquinolones, trimethoprim/sulfamethoxazole, and piperacillin/tazobactam [18]. In ETA culture, E. meningoseptica was isolated 12 times. In our study, three isolates were sensitive to quinolones, nine isolates were sensitive to ceftazidime-avibactam alone, and all other isolates in the culture antibiogram were resistant. In intensive care units, infection control measures must be rigorously implemented. In order to prevent infections, daily patients should have their VAP prevention bundles filled on a regular basis. In addition, antibiotic administration should adhere to a defined antibiotic management program.

In neonatal and pediatric patients, the mortality rate owing to E.meningoseptica ranged from 12.5% to 66.7% [19]. In an adult intensive care unit study, the mortality rate of VAP was 16.6%, 6.6% due to E.meningoseptica, and the cause of death in these patients was not found to be infection-related [17]. The agent was isolated from the tracheal aspirate cultures of nine out of nineteen patients who were ventilated mechanically, and four of these patients died [20]. In our study, VAP-related E. meningoseptica mortality was 2.3%, while VAP-related E. meningoseptica mortality was 19%. Even though mortality was not high in our study, inappropriate antibiotic use and the avoidance of superfluous central venous catheter placement are crucial for the eradication of E.meningoseptica infection. Given the prevalence of antimicrobial resistance, the lower mortality may be attributable to the increased use of newer antibiotic options, swift microbiological diagnostic tests, or antimicrobial susceptibility tests. Mortality may have decreased over time due to the enhanced conditions of pediatric intensive care units, rapid diagnosis, and early treatment. Healthcare professionals can play a crucial role in preventing and managing Elizabethkingia meningoseptica infections by maintaining infection control measures, improving antibiotic stewardship, and collaborating with infectious disease specialists to ensure appropriate diagnosis and treatment.

Our research had several limitations. The investigation was conducted retrospectively at a single center with a small sample size. There is a need for prospective and controlled investigations.

Conclusion

In recent years, the prevalence of E. meningoseptica infection has increased dramatically, producing fatal opportunistic infections in patients. In recent years, E. meningoseptica has been isolated more frequently in pediatric intensive care units from patients who use broad-spectrum antibiotics, are followed up with a central venous catheter, have prolonged mechanical ventilation, and have lengthy hospital stays. The high level of resistance to the majority of broad-spectrum antibiotics makes its management difficult. Emerging nosocomial pathogen E. meningoseptica is difficult to treat due to its high antimicrobial resistance, prolonged mechanical ventilation duration, and intensive care unit hospitalization in pediatric patients. A multifaceted strategy is required to prevent Elizabethkingia meningoseptica infections in critically ill pediatric patients. Proper hand hygiene and infection control measures, such as routine cleansing and disinfection of hospital surfaces and equipment, can aid in reducing the risk of transmission. Additionally, identifying and treating any underlying medical conditions or risk factors can aid in preventing infections. Future research should focus on the risk factors and treatment of E. meningoseptica infection.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
The authors declare no conflict of interest.

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